

## IN THE SPECIFICATION

Please replace the paragraph beginning at page 4, line 5, with the following rewritten paragraph:

Fig. 1 (SEQ ID NO:13) is a schematic drawing of a target-cleaving ribozyme sequence of the invention for CCR5;

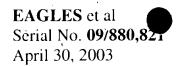
Please replace the paragraph beginning at page 4, line 7, with the following rewritten paragraph:

Figs. 2 (SEQ ID NO:14) and 11 (SEQ ID NO:15) are schematic drawings of target-cleaving ribozymal DNA sequences linked to a 3'-autocatalytic sequence to provide a double hammerhead ribozymal DNA for targeting CCR5 and CXCR4 mRNA, respectively;

Please replace the paragraph beginning at page 4, line 10, with the following rewritten paragraph:

Figs. 3 (SEQ ID NO:5) and 12 (SEQ ID NO:8) show the DNA sequences of cassettes comprising the ribozymal DNA of Figs. 2 and 11 (SEQ ID NO:14) and (SEQ ID NO:15), driven by a T7 promoter;

Please replace the paragraph beginning at page 4, line 12, with the following rewritten paragraph:





Figs. 4a (SEQ ID NO:1) and 4b (SEQ ID NO:2) are schematic drawings of targetcleaving ribozyme sequences used in this invention, in relation to CCR5 and CXCR4 mRNA targets;

## IN THE CLAIMS

The following claim set replaces all prior versions, and listings, of claims in the application:

1. (previously amended) A vector system comprising at least one DNA vector, the vector or vectors containing a target-cleaving hammerhead ribozymal DNA sequence under control of a promoter effective in human cells and which, upon transcription to RNA will cleave the mRNA transcribed from a target gene encoding the CCR5 or CXCR4 protein, the target-cleaving ribozymal DNA sequence, when transcribed to RNA, cleaving a target RNA sequence present in CCR5 or CXCR4 RNA, and which contains a first recognition sequence (5' to 3'):

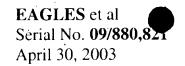
tagattg or ctcact, respectively for CCR5 and CXCR4 and downstream thereof a second recognition sequence

acttg or acgttgt, respectively for CCR5 and CXCR4.

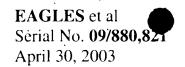
2. (original) A vector system according to Claim 1, containing target-cleaving ribozymal sequences for cleaving mRNA transcribed from both the CCR5 and CXCR4 target genes.

- 3. (previously mended) A vector system according to Claim 1, comprising at least two DNA vectors, wherein a first vector contains a first promoter effective in human cells, operably linked to a gene which is expressible to produce an activator protein capable of acting on a second promoter, and a second vector contains the second promoter operably linked to a target-cleaving hammerhead ribozymal DNA sequence for cleaving mRNA transcribed from the CCR5 target gene, the CXCR4 target gene or both the CCR5 and CXCR4 target genes.
- 4. (original) A vector system according to Claim *3*, comprising at least 3 DNA vectors, wherein the second vector contains target-cleaving ribozymal DNA for cleaving mRNA transcribed from the CCR5 target gene and wherein the third vector contains target-cleaving ribozymal DNA for cleaving mRNA transcribed from the CXCR4 target gene.
- 5. (previously amended) A vector system according to Claim 3, wherein the second promoter is a T7 polymerase promoter and the activator protein is a T7 polymerase.
- 6. (currently original) A vector system according to Claim 5, wherein the <u>T7</u> polymerase promoter further comprises DNA providing an internal ribosome entry site (IRES) for assisting the translation of the T7 polymerase gene in human cells.

- 7. (previously amended) A vector system according to claim 1 wherein the ribozymal DNA sequence further comprises, downstream of the target-cleaving ribozymal sequence, a 3'-autocatalytic hammerhead ribozymal DNA sequence. so that when the ribozymal DNA is transcribed to RNA, it has a representable form as a double hammerhead, having first and second stems of a target-cleaving ribozyme which targets CCR5 or CXCR4 mRNA and first and second stems of 3'-autocatalytic ribozyme.
- 8. (currently amended) A vector system according to claim 1, wherein the first and second structure-stabilising stem loops are positioned one to each side of the first recognition sequence.
- 9. (original) A vector system according to Claim 8, wherein a second recognition sequence is positioned downstream of the second structure-stabilising stem loop.
- 10. (original) A vector system acid according to Claim 9, wherein the targetcleaving ribozyme sequence comprises in order (5' to 3'):
  - a first structure-stabilising stem loop;
  - a first target-recognition sequence;
  - a first catalytic sequence;
  - a second structure-stabilising stem loop;
  - a second catalytic sequence; and
  - a second target-recognition sequence.



- 11. (cancelled).
- 12. (previously amended) A pharmaceutically acceptable carrier containing a vector system defined in claim 1.
  - 13. (original) A carrier according to Claim 12 in the form of liposomes.
- 14. (original) A pharmaceutical composition comprising lipsomes as claimed in Claim 13 and a diluent or carner.
  - 15-16. (cancelled).
- 17. (previously amended) Ribozymal DNA comprising (1) a target-cleaving hammerhead ribozymal DNA sequence under control of a promoter effective in human cells and which, upon transcription to RNA will cleave the mRNA transcribed from a target gene encoding the CCR5 or CXCR4 protein, and downstream thereof (2) a 3'-autocatalytic hammerhead ribozymal DNA sequence, so that when the ribozymal DNA is transcribed to RNA, it has a form represented as a double hammerhead, having first and second steps of a target-cleaving ribozyme which targets CCR5 or CXCR4 mRNA and first and second stems of 3'-autocatalytic ribozyme, together with a common third stem joining the two hammerheads, the target-cleaving ribozymal DNA sequence, when transcribed to RNA, cleaving a target RNA sequence present in CCR5 or CXCR4 RNA, and which contains a first recognition sequence (5' to 3'):



tagattg or ctcact, respectively for CCR5 and CXCR4 and downstream thereof a second recognition sequence

acttg or acgttgt, respectively for CCR5 and CXCR4.

18. (original) Ribozymal DNA which, when transcribed to RNA, will cleave a target RNA sequence present in CCR5 or CXCR4 RNA and which contains a first recognition sequence (5' to 3'):

tagattg or ctcact, respectively for CCR5 and CXCR4 and downstream thereof a second recognition sequence acttg or acgttgt, respectively, for CCR5 and CXCR4.

- 19. (original) Ribozymal DNA according to Claim 18, comprising tandem CCR5 RNA- and CXCR4 RNA- cleaving sequences.
- 20 (new). A method of therapy against human immunodeficiency virus infection which comprises administering to a subject in need thereof an effective amount of a vector system as defined in Claim 1.
- 21 (new). A method of therapy against human immunodeficiency virus infection which comprises administering to a subject in need thereof an effective amount of a vector system as defined in Claim 2.